

Appendix A. Amended Claims.

1. (currently amended) A compound for inhibiting the toxicity of an amyloid protein or amyloid peptide, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least four modified or unmodified amino acids; said compound comprising a peptidyl sequence selected from the group consisting of:

$X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-(S)_n$;

$(S)_n-X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}$;

$Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-(S)_n$;

$(S)_n-Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}$;

$X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3}-(S)_n$;

$(S)_n-X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3}$;

$Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}-(S)_n$;

$(S)_n-Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}$;

$X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3}-Y_{AA3}-(S)_n$;

$(S)_n-X_{aa1}-Y_{AA1}-X_{aa2}-Y_{AA2}-X_{aa3}-Y_{AA3}$;

$Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}-X_{aa3}-(S)_n$;

and

$(S)_n-Y_{AA1}-X_{aa1}-Y_{AA2}-X_{aa2}-Y_{AA3}-X_{aa3}$;

wherein:

- (a) X_{aa1} , X_{aa2} , and X_{aa3} are natural or synthetic amino acids that are identical or homologous to alternating amino acids of the aggregation-inducing sequence of the amyloid protein or amyloid peptide, and that have side chains adapted for cross-strand side chain interactions with a β -sheet;
- (b) Y_{AA1} , Y_{AA2} , and Y_{AA3} are natural or synthetic amino acids that are identical or homologous to alternating amino acids of the aggregation-inducing sequence of the amyloid protein or amyloid peptide; wherein Y_{AA1} , Y_{AA2} , and Y_{AA3} correspond to amino acids that will be positioned on opposite faces of a β -sheet containing the amino acids that correspond to X_{aa1} , X_{aa2} , and X_{aa3} ; and wherein the amino acids in the amyloid protein or amyloid peptide that correspond to X_{aa1} , X_{aa2} , and X_{aa3} alternate with the amino acids in the amyloid protein or amyloid peptide that correspond to Y_{AA1} , Y_{AA2} , and Y_{AA3} ; wherein at least two of Y_{AA1} , Y_{AA2} , and Y_{AA3} are $C^{\alpha,\alpha}$ -disubstituted amino acids;
- (c) $(S)_n$ is a hydrophilic region consisting of comprising hydrophilic amino acids or other hydrophilic groups; wherein n is from 4 to 10, and wherein said hydrophilic region has a size not larger than about the size of a decapeptide;
- (d) either or both ends of said peptidyl sequence optionally comprise additional functionality that does not adversely affect the compound's ability to inhibit the toxicity of an amyloid protein or amyloid peptide, as compared to an otherwise identical compound lacking such additional functionality; [[and]]
- (e) the number of amino acids in the aggregation sequence of the amyloid protein or amyloid peptide may be the same as, or different from, the number of natural or synthetic amino acids in said peptidyl sequence; and

(f) if the aggregation-inducing sequence contains, as alternating amino acids, either the sequence Lys-Val-Phe or the sequence Leu-Phe-Ala, then X_{aa1} , X_{aa2} , and X_{aa3} are identical neither to the sequence Lys-Val-Phe nor to the sequence Leu-Phe-Ala.

2 - 3. (canceled).

4. (previously presented) The compound of Claim 1, wherein said compound is (Lys)₇-Dibg-Val-Dbzg-Phe-Dpg-NH₂ (SEQ ID NO: 5).

5 - 6. (canceled)

7. (original) The compound of Claim 1, wherein the aggregation-inducing sequence is selected from the group consisting of KLVFFA (SEQ ID NO: 3); FLVHS (SEQ ID NO: 9); NFLVH (SEQ ID NO: 10); NFGAIL (SEQ ID NO: 11); VGGAVVTGV (SEQ ID NO: 12); VNITIKQHTVTTT (SEQ ID NO: 13); LANFLV (SEQ ID NO: 14); FLVHSS (SEQ ID NO: 15); AGDV (SEQ ID NO: 16); and Q_m; wherein m is an integer from 25 to 45.

8. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is KLVFFA (SEQ ID NO: 3).

9. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is FLVHS (SEQ ID NO: 9).

10. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is NFLVH (SEQ ID NO: 10).

11. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is NFGAIL (SEQ ID NO: 11).

12. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is VGGAVVTGV (SEQ ID NO: 12).

13. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is GAV.

14. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is VNITIKQHTVTTTT (SEQ ID NO: 13).

15. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is LANFLV (SEQ ID NO: 14).

16. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is FLVHSS (SEQ ID NO: 15).

17. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is AGDV (SEQ ID NO: 16).

18. (original) The compound of Claim 7, wherein the aggregation-inducing sequence is Q_m; wherein m is an integer from 25 to 45.

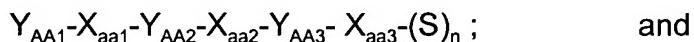
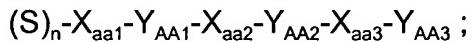
19. (canceled)

20. (original) The compound of Claim 1, wherein each of Y_{AA1}, Y_{AA2}, and Y_{AA3} is an C^{α,α}-disubstituted amino acids.

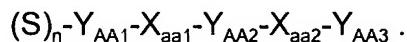
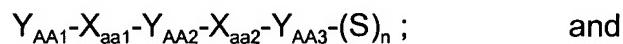
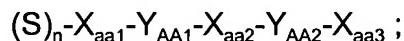
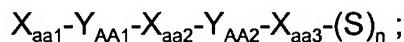
21. (original) A composition of matter comprising the compound of Claim 1, and a pharmaceutically acceptable carrier.

22 - 50 (canceled)

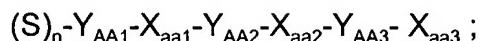
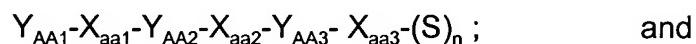
51. (previously presented) A compound as recited in Claim 1, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least six modified or unmodified amino acids, and wherein said peptidyl sequence is selected from the group consisting of:



52. (previously presented) A compound as recited in Claim 1, wherein the amyloid protein or amyloid peptide comprises an aggregation-inducing sequence of at least five modified or unmodified amino acids, and wherein said peptidyl sequence is selected from the group consisting of:



53. (previously presented) A compound comprising a peptidyl sequence selected from the group consisting of:



wherein:

(a) X_{aa1} is L-lysine or D-lysine, X_{aa2} is L-valine or D-valine, and X_{aa3} is L-phenylalanine or D-phenylalanine;

(b) Y_{AA1} is a $C^{\alpha,\alpha}$ -disubstituted amino acid analog of leucine, Y_{AA2} is a $C^{\alpha,\alpha}$ -disubstituted amino acid analog of phenylalanine, and Y_{AA3} is a $C^{\alpha,\alpha}$ -disubstituted amino acid analog of alanine; and

(c) $(S)_n$ is a hydrophilic region comprising hydrophilic amino acids or other hydrophilic groups.

54. (previously presented) The compound of Claim 53, wherein said compound is Lys-Dibg-Val-Dbzg-Phe-Dpg-(Lys)₆-NH₂ (SEQ ID NO: 4).

55. (previously presented) The compound of Claim 1, wherein n is from 4 to 6.

56. (new) The compound of Claim 1, wherein at least two of Y_{AA1} , Y_{AA2} , and Y_{AA3} are $C^{\alpha,\alpha}$ -disubstituted amino acids.